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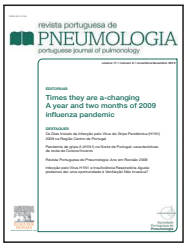

ORIGINAL ARTICLE

Respiratory muscle strength and quality of life in myotonic dystrophy patients

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KEYWORDS
Maximal respiratory pressures;
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Abstract
Introduction: Studies on quality of life in myotonic dystrophy (MD) are scarce and the relationship between respiratory muscle strength and health-related quality of life (HRQoL) has yet to be determined. The present study aims to investigate respiratory muscle strength and HRQoL and their relationship in MD patients.
Methods: Twenty-three patients (13 men, aged 40 ± 16 years) with MD were evaluated for pulmonary function, maximal inspiratory and expiratory pressure (MIP and MEP, respectively), sniff nasal inspiratory pressure (SNIP) and HRQoL using the Short Form (SF-36) quality of life questionnaire.
Results: Respiratory muscle strength values were 71 ± 20 cmH_2O (64%predicted), 76 ± 32 cmH_2O (70%predicted), and 79 ± 28 cmH_2O (80%predicted) for MEP, MIP, and SNIP respectively. Significant differences were found in the SF-36 domains of physical functioning 58.7 ± 31.4 *vs* 84.5 ± 23 ($P < 0.01$, 95%CI = 1.6-39.9) and physical problems 43.4 ± 35.2 *vs* 81.2 ± 34 ($P < 0.001$, 95%CI = 19.4-6.1) when compared with the reference values. According to single linear regression analysis, MIP explains 29%of the variance in physical functioning, 18%of physical problems and 20%of vitality.
Conclusions: Individuals with MD have reduced expiratory muscle strength. HRQoL may be more impaired in some physical domains, which might be influenced by variations in inspiratory muscle strength.

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PALAVRAS-CHAVE
Pressões respiratórias máximas;
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Doença neuromuscular;
SF-36;
Músculos respiratórios

Força muscular respiratória e qualidade de vida em pacientes com distrofia miotonica

Resumo
Introdução: Na distrofia miotônica (DM) estudos sobre qualidade de vida relacionada à saúde (QVRS) ainda são escassos e a sua relação com a força muscular respiratória não foi determinada. Este estudo teve como objetivo a avaliação da força muscular respiratória e da QVRS, além de determinar as relações entre estas variáveis na DM.
Métodos: Foi avaliada a função pulmonar, as pressões respiratórias máximas inspiratórias e expiratórias (PImáx e PEmáx, respectivamente), pressão nasal inspiratória de *sniff* (SNIP), e a QVRS através do questionário genérico SF-36 em 23 pacientes (13 homens, idade 40 ± 16 anos) com DM.
Resultados: Os valores encontrados da força muscular respiratória foram de 71 ± 20 cmH_2O (64% preditivo), 76 ± 32 cmH_2O (70%preditivo), e 79 ± 28 cmH_2O (80%preditivo) para PEmax, PImax e SNIP respectivamente. Encontramos diferenças significativas nos domínios de SF-36 de função física 58,7 ± 31,4 *vs.* 84,5 ± 23 ($p < 0,01$, 95%CI = 1,6 —39,9) e problemas físicos 43,4 ± 35,2 *vs.* 81,2 ± 34 ($p < 0,001$, 95%CI = 19,4 —6,1) comparado com os valores de referência. A analise de regressão linear demonstrou que a PImax explica 29%da variação da função física, 18%dos problemas físicos e 20%da vitalidade.
Conclusão: Indivíduos com DM têm uma redução da força muscular expiratoria. A QVRS pode ser mais prejudicada em alguns domínios da atividade física, o que pode sofrer influência das variações da força muscular inspiratória.

Introduction

Myotonic dystrophy (MD) is an autosomal dominant neuromuscular disease. The condition is characterized by myotonia, varying degrees of muscle weakness and systemic manifestations such as cataracts, endocrinal disorders, sleep disorders, hair loss and cardiac conduction disturbances[1]. It is the most common dystrophy in adults, with an incidence of 1/8000 births and prevalence of 1/20000 inhabitants.[1,2] Muscle weakness progression commonly occurs in muscles distal to proximal,[3] with the involvement of the respiratory muscles in middle age.[4]

Approximately half of MD-related mortality is due to respiratory complications, mainly pneumonia or respiratory failure.[3] Respiratory muscle weakness has a fundamental role in the pathogenesis of chronic respiratory failure, which is more prevalent in the last stages of the disease when the proximal muscles are affected. However, there are reports of decreased respiratory muscle strength in the first phases of MD, with the onset of respiratory failure occurring earlier.[5]

Decline in respiratory muscle strength is rehabilitable and requires specific assessment. Forced vital capacity (FVC) is one of the most widely used noninvasive methods for evaluating neuromuscular diseases although its values may not fall when respiratory muscle weakness is not pronounced. Maximal expiratory and inspiratory pressure (MEP and MIP) have been used to identify the risk of respiratory failure and predict survival in patients with neuromuscular diseases.[6] However, these maneuvers can be difficult to execute or interpret when the lips do not close properly around the mouthpiece, as in the case of orofacial weakness.[7] Sniff nasal inspiratory pressure (SNIP) is a recent noninvasive test developed to assess inspiratory muscle strength and is obtained through the sniff test. It does not require a mouthpiece and therefore makes patient evaluation easier. SNIP is considered an alternative complementary method to MIP, achieving higher values in healthy individuals and in neuromuscular diseases.[7-9] However, few studies have applied MIP and SNIP concomitantly on patients with MD, even though their combined use could help reduce false diagnoses of inspiratory muscle weakness.[8]

Earlier studies show that health-related quality of life (HRQoL) in MD may be severely compromised by chronicity and the duration of the neuromuscular diseas.[10,11] Similarly, the presence of respiratory muscle weakness in MD has been well established.[5,12,13] However, there are no studies on the relationship between respiratory muscle strength (MIP, MEP and SNIP) and HRQoL in MD. This study aimed to investigate respiratory muscle strength and HRQoL, and the relationship between the two, in a sample of patients with MD.

Methods

Patients

Patients diagnosed with MD without cardiac, respiratory or musculoskeletal comorbidities and monitored by a neurologist, were invited to participate in the study. The

diagnosis was based on clinical signs, electromyography (EMG) and family history. Subjects were selected at an ambulatory visit, after which the level of muscle compromise, pulmonary function, respiratory strength and HRQoL were assessed. The study was approved by the hospital Ethics Committee and all patients gave informed consent under protocol 151/07.

Assessment measures

Degree of muscle impairment: all participants were classified by the neurologist according to the Muscle Impairment Rating Scale (MIRS), an MD-specific scale. There are five degrees of impairment in relation to muscle involvement, progressing from distal to proximal: grade 1, no muscular impairment; grade 2, minimal signs (myotonia, jaw and temporal wasting, facial weakness, neck flexor weakness, ptosis, nasal speech, no distal weakness except isolated digit flexor weakness); grade 3, distal weakness (no proximal weakness except isolated elbow extensor weakness); grade 4, mild to moderate proximal weakness; grade 5, severe proximal weakness.[14]

Pulmonary function: the technical procedure, acceptability and reproducibility criteria, as well as standardization for measure were in accordance with the Brazilian Thoracic Association.[15] The DATOSPIR 120 spirometer (Sibelmed®, Barcelona, Spain) was used to measure FEV_1 and FVC. Three reproducible maneuvers were performed and the one with the best curve was considered for the study. Predicted values were those described from pre-established equations.[16]

Respiratory muscle strength: maximal respiratory pressures were measured in accordance with Black and Hyatt and the Brazilian Thoracic Association,[15,17] using reference values obtained from the Brazilian population.[18] MIP was measured with the subjects in a seated position and the nostrils occluded, at RV and MEP at TLC. Between five and eight maneuvers were carried out until two maximal values were reproducible. The sniff test was measured in an occluded nostril during a maximal sniff through the contralateral nostril. A plug with an orifice of around 1 mm coupled to a catheter was connected to a hand-held MicroRPM® (MICRO Medical®, Rochester, Kent, UK) pressure meter. Ten measures were taken and the result with the highest value was selected.[19] Reference values were obtained from equations described by Uldry and Fitting.[20] The cut-off points for diagnosing weakness described in the literature were used for both maximal respiratory pressures and SNIP. The values for men and women were: MIP 45 and 30 cmH_2O; MEP 80 and 60 cmH_2O and SNIP 50 and 45cmH_2O[8], respectively.

Health-related quality of life: was assessed using the Medical Outcomes Study Short Form-36 (SF-36), a generic questionnaire evaluating quality of life in relation to different diseases and in a healthy population. The present study applied the translated version with its psychometric properties tested and approved,[21] adapted to Portuguese for the Brazilian population.

Statistical analysis

Descriptive analysis was conducted after determining the means and standard deviation of the parameters age, body mass index (BMI), time of diagnosis, FVC (% predicted), FEV_1 (%predicted) and FEV_1/FVC, as well as respiratory muscle strength variables and the domains of the SF-36 questionnaire. Normal distribution of data and homogeneity were tested using the Kolmogorov-Smirnov. Statistical analyses were carried out using Pearson's correlation and the Student's t-test. The latter was performed to compare the SF-36 results of patients and healthy individuals. Linear regression analysis was used to study the relationship between the domains of quality of life that were significantly correlated with respiratory muscle strength variables. A P value of < 0.05 was considered to be significant. Statistical Package for Social Sciences for Personal Computers (SPSS/PC, version 15.0) was used.

Results

Between September and December 2007, 25 patients (13 men) were recruited for the study. Two patients did not complete the study due to difficulty understanding the tests or questionnaire. Patient characteristics, time of diagnosis, muscle impairment scale degree and spirometric measures are shown in Table 1. MIRS results revealed that 13%(n = 3) of the patients were classified as grade 1, 47% (n = 11) as grade 2, 17.4%(n = 4) as grade 3 and 21.7% (n = 5) as grade 4, and no patients as grade 5. Mean age of patients in grades 1 to 4 was 67 ± 9, 36 ± 14, 26 ± 5 and 42 ± 8, respectively. Pulmonary function showed a mild restrictive pattern.

The respective mean values of MEP, MIP and SNIP were 71 ± 20 cmH_2O—64% predicted, 76 ± 32 cmH_2O—70% predicted and 79 ± 28 cmH_2O—80%predicted. A progressive decrease in MEP%predicted values independent of gender, was correlated to MIRS classification of muscle impairment. The MEP%predicted was 81%in grade 1 MIRS, 71%in grade 2 MIRS, 60%in grade 3 MIRS and 45%in grade 4 MIRS.

Table 1 Patient characteristics, degree of muscle impairment and pulmonary function

Characteristics	Patients
Sex, M/F	13/10
Age, years	40 ± 16*
BMI, kg/m^2	23.1 ± 5.3*
Time of diagnosis, years	8.4 ± 7.3*
MIRS, grades 1/2/3/4/5	3/11/4/5/0
FVC, %pred	77.4 ± 13*
FEV_1, %pred	77 ± 13*
FEV_1/FVC, %	83.5 ± 7.4*

BMI indicates body mass index; F, female; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; M, male; MIRS, Muscular Impairment Rating Scale - 1 = no muscular impairment, 2 = minimal signs, 3 = distal weakness, 4 = mild or moderate proximal weakness, 5 = severe proximal weakness.
*Values in mean ± SD.

A total of 52%(n = 12, 8 male) of patients presented mean MEP values below the cut-off point (Figure 1). Only one subject (male) classified as grade 4 presented with MIP lower than the cut-off point for weakness, however, SNIP values were above the cut-off point. Patients rated as grade 1 showed results below 60%of the predicted. Three patients classified in grade 2, one in grade 3 and four in grade 4 had MIP values below 60%of predicted. MEP was below 60%of predicted in three patients classified in grade 2, two in grade 3 and all grade 4 patients. In relation to SNIP, one patient from each grade had values below 60% of predicted. In absolute numbers, the relation between MIP and MEP was reduced. In healthy subjects MEP was approximately double that of MIP.[22] This result is different from that seen in patients with MD, as illustrated in Figure 2.

With respect to HRQoL, the values found for most of the domains, except mental health, were less than the reference values for a healthy population[23]. There was a statistically significant difference for the domains physical functioning ($P = 0$, 95%CI = 19.7-39) and physical problems ($P = 0$, 95%CI = 28-56) (Table 2). Lower MIRS scores were obtained from patients in grade 1. These showed higher mean age for the physical functioning domain with a score of 28.3. MIRS scores for subjects in grade 4 were also reduced for the physical problems domain with a mean score of 30.

Relationships between respiratory muscle strength and HRQoL showed a positive correlation between MIP and the physical functioning, physical problems and vitality domains (Figure 3). No correlation was observed between the other respiratory muscle variables and SF-36 domains. Single linear regression analysis established that MIP explains 29%of the variance in physical functioning, 18%in physical problems and 20%in vitality.

Discussion

The main findings of the study were: 1) MD patients showed loss of expiratory muscle strength and patients with a worse MIRS grade had further decrease in MEP and 2) some HRQoL domains correlated with inspiratory muscle strength and 3) MD patients displayed impairment in the physical functioning domains of general health related quality of life.

HRQoL is a term used to define values attributed by individuals, in which life can be altered by functional states, perceptions, infirmities or treatment.[24] Individuals with neuromuscular diseases may have compromised quality of life due to both physical and psychosocial factors.[25,26] Individuals with MD have similar complaints to patients with other neuromuscular diseases and their quality of life is significantly associated with the capacity to walk, move and perform manual tasks.[27] When assessing HRQoL using the SF-36 questionnaire, our patients achieved worse results in nearly all domains, except mental health, when compared to quality of life values in healthy subjects. Antonini et al.[10] and Ford et al.[11] used the SF-36 questionnaire in studies with 20 and 21 patients, respectively. They determined that patients may obtain worse results in all quality of life domains, primarily in those related to physical and mental

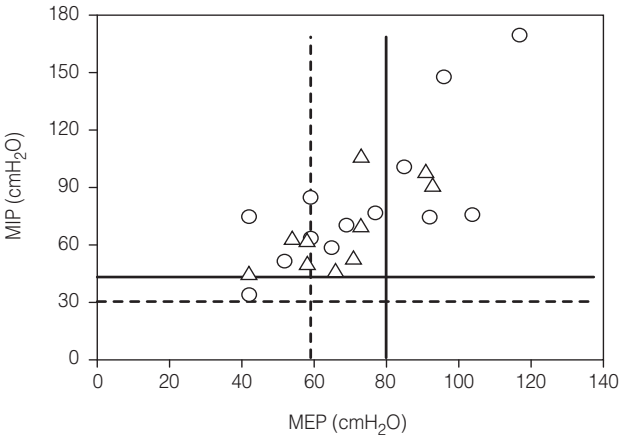

Figure 1 Maximal Respiratory Pressure: solid line represent cut off point of MIP and MEP to males. Dashed line represent cut off point of MIP and MEP for females. Circles represented males and triangles represented females. MEP indicates expiratory pressure; MIP, maximal inspiratory.

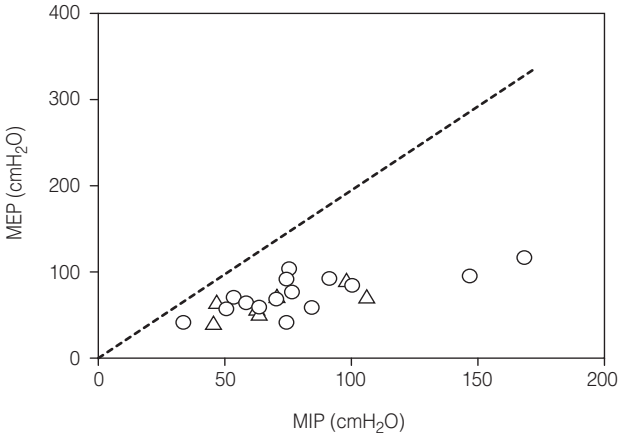

Figure 2 Relationship between maximal inspiratory and expiratory pressure in MD patients. Circles represented males and triangles represented females. Dotted line represent expected MEP/MIP relation between found in healthy subjects. MEP indicates expiratory pressure; MIP, maximal inspiratory.

Table 2 Health-related quality of life in patients and healthy reference values

SF-36 domains	Patients	Healthy controls[a]
Physical functioning	58.7 ± 31.4	88 ± 23.3[b]
Physical problems	43.4 ± 35.2	85.3 ± 34[b]
Bodily pain	71.3 ± 29	76.6 ± 23.7
General health perception	63.3 ± 21.6	74.2 ± 20.3
Vitality	59 ± 21.4	62.6 ± 21
Social aspects	71 ± 31.7	84.8 ± 22.7
Emotional aspects	68.4 ± 36	82.8 ± 33
General mental health	74.7 ± 18	75.3 ± 18.1

[a]Zung WK. Arch Gen Psychiatry. 1965. [b]$P < .001$. Patients versus healthy subjects. Values expressed in mean ± SD.

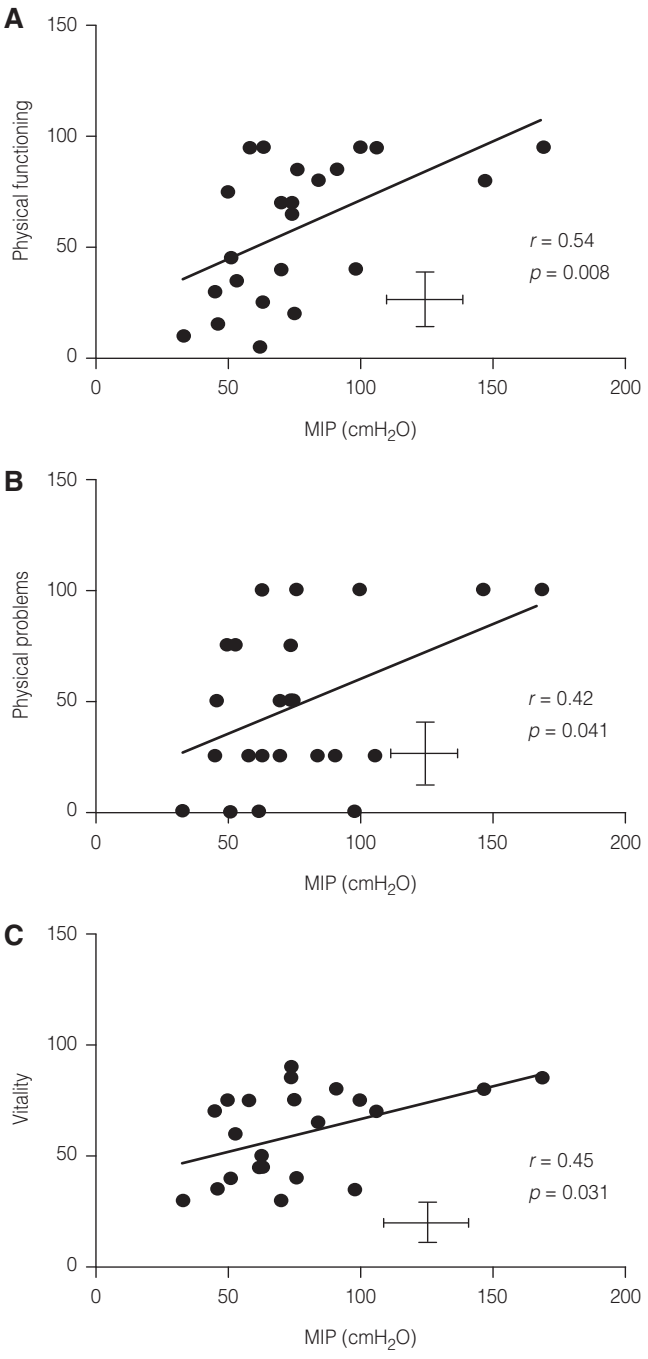

Figure 3 Correlation between MIP and: (A) physical functioning; (B) physical problems; (C) vitality. MIP indicates maximal inspiratory.

activity and bodily pain,. In the same study, Antonini et al.[10] found an inverse correlation between age, disease duration and severity in domains related to both physical and mental health. This finding leads us to hypothesize about the role of the disease on the perception of quality of life in patients with MD.

The association between measures of quality of life and respiratory function has been extensively investigated in studies on chronic respiratory diseases. Previous studies found a strong relationship between respiratory muscle strength, lung function and quality of life in neuromuscular disease.[27] This was studied by Ahlström et al.,[28] who assessed 57 individuals with muscular dystrophies, 32 of these with MD. Respiratory muscle strength was not assessed, but 41%of the patients with MD had moderately or severely reduced FVC and a direct relationship between reduced quality of life and decline in respiratory function. In the present study, patients showed mildly reduced FVC and a significant decrease in respiratory muscle strength compared to predicted values. We also found a relationship between MIP and the HRQoL domains of physical functioning, physical problems and vitality. Based on our results, it is suggested that MIP may have a predictive value with respect to the physical dimension of quality of life.

Our MD subjects demonstrated low expiratory muscle strength values even though most patients exhibited minimal signs of muscle impairment. This supports the idea that respiratory muscle weakness may also be present in the absence of clear weakness in the proximal limb muscles. These results suggest that the expiratory muscles can be affected before other muscle alterations occur and emphasize the importance of continuously assessing respiratory muscles. It also supports the view that the respiratory muscles are the origin of other pulmonary complications caused by neuromuscular diseases, since respiratory muscle function was altered even in patients with normal or partially preserved pulmonary function. Among the studies assessing muscle and pulmonary function in MD patients are those conducted by Ugalde et al.[12] with 10 predominantly male patients and Zifko et al.[13] on 25 patients with MD. Both observed a pulmonary function pattern with slight restriction, similar to that found in our study. However, respiratory muscle strength was further impaired when compared to our data. Despite similar results in lung function, patients in these studies were not classified using the MIRS scale. Comparisons with our results are therefore difficult to make, given that the relationship between the functional alterations in peripheral muscles and the loss of respiratory muscle strength were not established by the authors.

The preferential involvement of the expiratory muscles, observed by the decline in MEP, was found in other studies.[5,29,30] Previous results[5] demonstrated that MD patients with proximal weakness may experience greater decrease in MIP values than in MEP. Our results showed that the reduction in MEP persists at an intermediate level of the disease, without signs of proximal weakness. Ugalde et al.[12] studied the electromyographic activity of abdominal muscles in MD, observing no expiratory muscle weakness. However, the sample studied was smaller and no distinction was made for the degree of muscle impairment. In contrast, Veale et al.[29] compared respiratory pattern during sleep and wakefulness in normal individuals, those with MD and those with neuromuscular diseases. They found that, despite a similar degree of respiratory muscle weakness in the two groups of patients, those with MD showed lower MEP in even a small sample (7 patients), without classifying the degree of muscle impairment. This was also observed by Finnimore et al.,[30] who investigated the presence of nocturnal hypoxemia

and its correlations with diurnal respiratory pulmonary and muscle function in 12 patients with MD. These authors showed a clear respiratory muscle dysfunction, primarily due to reduced MEP.

Recent studies observed that SNIP values were greater than those of MIP in both healthy individuals and those with neuromuscular diseases.[7,20] Our results show that approximately half of the patients had SNIP above MIP. Variability in the results is similar to that observed by Terzi et al.,[31] in which SNIP was higher than MIP in 48% of the patients with MD. These authors report that when SNIP values are greater than those of MIP, they may be used as the only measure to accompany muscle strength in neuromuscular patients. In other instances, MIP should also be assessed. Despite this suggestion, studies in the literature report that these maneuvers are not the same since the muscle activation pattern is different. This makes them complementary measures[9]. In MD patients with sleep-related respiratory disorders, Kumar et al.[2] recorded a tendency towards SNIP reduction when compared to MIP. This is a common problem in these patients. Our findings suggest the need for both tests (SNIP and MIP), since results may vary.

A potential limitation of our study is the small sample size due to the limited time and few resources available during the study period. However, the results of this study add new perspectives in terms of respiratory alterations and HRQoL in MD patients.

Conclusion

The results of the present study show that patients with MD have reduced expiratory muscle strength. Their HRQoL compared to healthy individuals may be more compromised in physical aspects, which may be influenced by variations in inspiratory muscle strength.

Conflict of interest

Authors declare they don't have any conflict of interest.

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